REMARKS/ARGUMENTS

Rejections under 35 U.S.C. § 102 and 103(a)

Claims 1, 17-26, 29-30, 32-39, and 44 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by, or alternatively under 35 U.S.C. § 103(a) as allegedly unpatentable over, Berg et al. (WO 95/01135). Applicants have carefully reviewed the instant rejection as well as the cited reference and respectfully traverse the rejection as failing to present a *prima facie* case of either anticipation or obviousness.

As an initial matter, Applicants respectfully point out that the rejection of claims 19-21 in the instant rejection appears to be at odds with the alleged rejection of the same claims in light of Berg et al. and Rouanet et al. (addressed below). Simply put, if Berg et al. discloses all the requirements of the subject matter of claims 19-21, as apparently alleged as part of the instant rejection, then why does the rejection based in part on Rouanet et al. state that Berg et al. fails to provide "disclosure on the specific density and surface area of the aerogels"? Applicants respectfully submit that Berg et al. do not provide a disclosure of subject matter as encompassed by claims 19-21 and so the rejection of these claims based upon Berg et al. alone is misplaced and should be withdrawn.

With respect to the first allegation of anticipation by Berg et al., Applicants respectfully point out that the rejected claims are directed to a dry aerogel powder as a vehicle for delivery of a therapeutic agent to alveoli as well as methods for the use of the powder in the treatment of a disease state and methods for the production of the powder. The teachings of Berg et al. are not sufficient, however, to anticipate the claims.

Simply put, Berg et al. do not teach or suggest a dry powder comprising a therapeutic agent capable of reaching alveoli. Berg et al. also do not teach or suggest any method of delivering a dry powder to alveoli. Reaching the alveoli is an express requirement of the claims. But Berg et al. do not even use the term "alveoli" or any derivative thereof.

As previously explained, the instant invention is based upon the formulation and use of aerogel particulates that are able to deliver therapeutic agents to the bloodstream via the lung of a subject. The particulates are able to do this by reaching the alveoli/alveolar sacs of the lung. This requires air borne movement through ever decreasing passages (through bronchus/bronchi to bronchioles and terminal bronchioles and then to respiratory bronchioles with occasional alveolar sacs with alveoli) with ever decreasing velocities. As noted on page 11, first paragraph, of the instant application, the air velocity approaches zero as the air reaches the alveoli. Air borne materials reaches the blood by diffusing through the alveolar epithelium, a thin interstitial space, and the capillary endothelium.

Berg et al., however, do not disclose or suggest any aerogel particles as capable of reaching the alveoli of lungs. The discussion on page 11, lines 31-35 through page 12, line 29, is directed to the use of aerogels as contrast agents in ultrasound imaging, which includes echocardiography, or the ultrasound examination of the heart and great vessels. Such aerogel formulations are not those used to deliver a therapeutic agent to the alveoli of lungs. Instead, the formulations are disclosed on page 12, lines 7-29, as containing "gas" which complements their use as contrast agents. As would be appreciated by the skilled person, aerogel particles loaded with "gas" would actually serve poorly as contrast agents in the air filled portions of the lungs, which are by definition filled with "gas".

The Berg et al. disclosure of using aerogels as contrast agents for X-ray (see page 12, line 30 to page 13, line 15) is also unrelated to delivery of a therapeutic agent to the alveoli of lungs because liver imaging and cardiovascular imaging are not concerned with the delivery of anything, much less a therapeutic agent, to alveoli. Similarly, bronchography (which relates to radiographic examination of the bronchial tree to diagnose bronchiectasis, or abnormal dilation of the bronchial) uses the administration of contrast medium (usually propyliodone in an oily or aqueous suspension) directly into the trachea or bronchi. This is physically distant and distinct from the deeper regions of the lungs where the alveoli are present. Additionally, the use of aerogel as the contrast agent in bronchography would accordingly be in some fluid or suspension rather than as a powder for delivery to the alveoli.

Therefore, Berg et al. do not disclose or suggest drug delivery to alveoli. The cited passages from page 14, line 15, to page 15, line 4 of Berg et al. do not alter this conclusion. Those passages describe possible combinations of an aerogel and various agents, none of which discloses the use of a dry powder as a vehicle for delivery of a therapeutic agent to alveoli. Instead, the bulk of the discussion concerns other modes of delivery such as "intracutaneous, subcutaneous, intramuscular, intravascular, intracardiac, intraspinal, intra-articular and ophthalmic routes" (see page 15, lines 9-12).

The discussion of "aerosol formulations" (page 15, lines 12-13) also fails to rescue the above deficiencies because there is no disclosure of the formulation being either a dry powder or being of appropriate density and physical size for delivery to alveoli as recited in the claims. Applicants thus respectfully submit that Berg et al. fail to disclose any aerogel or method that meets all the elements of the claimed invention as required by the standard set forth at MPEP 2131 and the cases cited therein.

In light of the above, Applicants respectfully submit that no *prima facie* case of anticipation has been presented and this aspect of the rejection may be properly withdrawn.

With respect to the allegation of obviousness in light of Berg et al., Applicants respectfully refer to the above discussion of the teachings of the reference, which includes the failure to teach or suggest the requirements of the claims relating to the ability to deliver a therapeutic agent to the alveoli. Therefore, and to establish a *prima facie* case, motivation to modify the teachings of Berg et al. to arrive at the claimed invention is necessary.

The statement of the rejection fails, however, to provide any such motivation. Instead, the statement of the rejection concludes with

> "it would have been obvious to one of ordinary skill in the art to have modified the teachings of Berg et al. to make and use the invention as claimed in the instant application because Berg et al. is providing sufficient disclosure to one of ordinary skill to make and use the

invention and to prepare light, effective, stable and non-toxic particles for drug delivery."

Applicants respectfully submit that the above fails to provide sufficient basis to support a *prima facie* case of obviousness because the logic of the assertion is circular. The conclusion is that it would have been obvious to modify Berg et al. to arrive at the claimed invention because

a) Berg et al. provides sufficient disclosure

b) to one of ordinary skill to make and use the invention

c) and to prepare light, effective, stable and non-toxic particles for drug delivery.

With respect to a), Applicants respectfully submit that even if Berg et al. provide a sufficient disclosure of their subject matter, it is irrelevant to the claimed invention the differences between that disclosure and the claimed subject matter (as discussed above with respect to the allegation of anticipation).

With respect to b), Applicants respectfully submit that the artisan of ordinary skill would not know to make materials for delivery to alveoli in the absence of the instant disclosure because Berg et al. neither teach or suggest such a concept. Thus this portion of the allegation appears to rely upon impermissible hindsight based on the instant application's disclosure.

With respect to c), Applicants respectfully submit that preparation of the above described particles is irrelevant given the failure to teach or suggest modification of the Berg et al. subject matter to address alveolar delivery.

In light of the above, Applicants respectfully submit that no *prima facie* case of obviousness has been presented and this aspect of the rejection may be properly withdrawn.

Claims 1, 17-18, and 22-44 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Berg et al. (as cited above) in light of Manning et al. (USP 5,981,474).

Applicants have carefully reviewed the instant rejection as well as the cited references and respectfully traverse the rejection as failing to present a *prima facie* case of obviousness.

As an initial matter, Applicants respectfully point out that Manning et al. fail to provide any teaching or suggestion of the subject matter in rejected claims 31, and 40-43. Because these claims were not included in the alleged rejection based upon Berg et al. alone (as discussed above), Applicants respectfully submit that these claims are not properly included in the instant rejection because of a failure to meet the standards set forth at MPEP 2143.03 and in the cases cited therein because not all claim limitations are taught at least with respect to claims 31, and 40-43.

With respect to the instantly rejected claims, the deficiencies of Berg et al. have been explained above, and the statement of the instant rejection does not remedy any part of those deficiencies. Instead, the instant rejection is simply directed to the inclusion of the teachings of Manning et al. with those of Berg et al. But Manning et al. also do not remedy the deficiencies of Berg et al.

Manning et al. further fail to provide any basis for combination with the aerogel based subject matter of Berg et al. Simply put, Manning et al. was cited for its discussion of insulin, methadone, and naltrexone without any mention or suggest of aerogel related technology to which Berg et al.'s disclosure is directed. Applicants respectfully submit that an artisan of ordinary skill would not combine Berg et al. and Manning et al. as alleged in the instant rejection. Moreover, Applicants respectfully submit that no expectation of success is provided for the modification of Berg et al.'s aerogel technology with the "hydrophobic ion pair complex with an amphiphillic material" technology of Manning et al.

Accordingly, Applicants respectfully submit that the combination of the two references is misplaced because no motivation or nexus for their combination has been presented. Moreover, no *prima facie* case of obviousness has been presented in light of the unaddressed deficiencies of Berg et al. Therefore, Applicants respectfully submit that this rejection is misplaced and may be properly withdrawn.

Claims 19-21 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Berg et al. (as cited above) in light of Rouanet et al. (USP 5,864,923). Applicants have carefully reviewed the instant rejection as well as the cited references and respectfully traverse the rejection as failing to present a *prima facie* case of obviousness.

The deficiencies of Berg et al. have been explained above, and the statement of the instant rejection does not remedy any part of those deficiencies. Instead, the instant rejection is simply directed to the inclusion of the teachings of Rouanet et al. with those of Berg et al. But Rouanet et al. also do not remedy the deficiencies of Berg et al.

Rouanet et al. was cited for its discussion of various aerogel properties without any mention or suggest of anything related to alveolar delivery of therapeutic agents. Thus even a combination of these teachings with those of Berg et al. would still not result in a dry powder as encompassed by the claims.

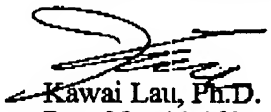
Accordingly, Applicants respectfully submit that no *prima facie* case of obviousness has been presented in light of the unaddressed deficiencies of Berg et al. Therefore, Applicants respectfully submit that this rejection is misplaced and may be properly withdrawn.

Conclusion

Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is urged.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6151 .

Respectfully submitted,



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Attachments
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